

On page 107, line 14, please delete "29" and insert in its place --32--.

On page 116, line 26, please insert --34-- immediately after ":".

On page 116, line 28, please insert --35-- immediately after ":".

On page 117, line 2, please insert --36-- immediately after ":".

On page 117, line 4, please insert --37-- immediately after ":".

On page 140, in Table 3, line 1, please insert --\*-- immediately after "Primers".

On page 141, in Table 3, line 1, please insert --\*-- immediately after "Primers".

On page 141, please insert --The PCR Primers correspond consecutively, in seriatum, to

SEQ ID NO: 39 through SEQ ID NO: 76.-- at the bottom of Table 3.

On page 142, in Table 4, please insert --\*-- immediately after "Primers".

On page 142, please insert --The Primers correspond consecutively, in seriatum, to SEQ

ID NO: 77 through SEQ ID NO: 92.-- at the bottom of Table 4.

On page 142, line 7, please insert --(SEQ ID NO: 93)-- immediately after  
"GGGAGCCTTGTCTGGGTACAAAG".

On page 149, line 13, please delete " \_\_ and \_\_ " and insert in its place --94 and 95--.

On page 155, line 16, please delete " \_\_ and \_\_ " and insert in its place --96 and 97--.

#### IN THE CLAIMS:

Please amend the claims as follows:

124. (Amended) A method for modifying the body weight of a mammal comprising administering a nucleic acid molecule encoding an OB polypeptide [according to claim 54] to the mammal under conditions that provide for expression of the OB polypeptide *in vivo*, such OB polypeptide capable of modulating body weight and selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in SEQ ID NO: 4;
- d) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;

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and

e) variants, including allelic variants, muteins, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.

Please add the following claims:

-- 132. A method according to claim 124 wherein said OB polypeptide variant is selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;  
b) amino acids 22-166 of SEQ ID NO: 5;  
c) SEQ ID NO: 6; and  
d) amino acids 22-166 of SEQ ID NO: 6.

D4  
133. A method according to claim 124 wherein said OB polypeptide has 83 percent or greater amino acid sequence homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5 or 6.

134. A method according to claim 124 wherein said OB polypeptide has one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166, according to the numbering of SEQ ID NO: 4, substituted with another amino acid.

135. A method according to claim 132 wherein said OB polypeptide has one or more of amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165, according to the numbering of SEQ ID NO: 6, substituted with another amino acid.

Sub 14  
136. A method according to claim 124 wherein said mammal is a mouse.

Handwritten notes: "E3" and "D4" are written vertically on the left margin. A box containing "I4" and "E3" is located near the top left. A diagonal line is drawn across the page from the top left to the bottom right.

137. A method according to claim 124 wherein said mammal is a human.

138. A method of delivering DNA encoding an OB polypeptide capable of modulating body weight to a mammal comprising administering to said mammal a vector which comprises such OB encoding DNA operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide by the mammal.

139. A method according to claim 138 wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in SEQ ID NO: 4;
- d) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;  
and
- e) variants, including allelic variants, muteins, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.

140. A method according to claim 139 wherein said OB polypeptide variant is selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;
- c) SEQ ID NO: 6; and
- d) amino acids 22-166 of SEQ ID NO: 6.

141. A method according to claim 138 wherein said OB polypeptide has 83 percent or greater amino acid sequence homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5 or 6.

142. A method according to claim 139 wherein said OB polypeptide has one or

*Sub E3*

more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166, according to the numbering of SEQ ID NO: 4, substituted with another amino acid.

143. A method according to claim 140 wherein said OB polypeptide has one or more of amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165, according to the numbering of SEQ ID NO: 6, substituted with another amino acid.

144. A method of expressing an OB polypeptide in a mammal comprising administering to said mammal a DNA vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence.

*D4*

145. A method according to claim 144 wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in SEQ ID NO: 4;
- d) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;
- and
- e) variants, including allelic variants, muteins, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.

146. A method according to claim 145 wherein said OB polypeptide variant is selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;
- c) SEQ ID NO: 6; and

*Sub E3*  
d) amino acids 22-166 of SEQ ID NO: 6.

147. A method according to claim 144 wherein said OB polypeptide has 83 percent or greater amino acid sequence homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4, 5 or 6.

148. A method according to claim 145 wherein said OB polypeptide has one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166, according to the numbering of SEQ ID NO: 4, substituted with another amino acid.

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149. A method according to claim 146 wherein said OB polypeptide has one or more of amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165, according to the numbering of SEQ ID NO: 6, substituted with another amino acid.

150. A method according to claim 144 wherein said DNA vector is a viral vector and is selected from the group consisting of attenuated or defective DNA virus vectors and retroviral vectors.

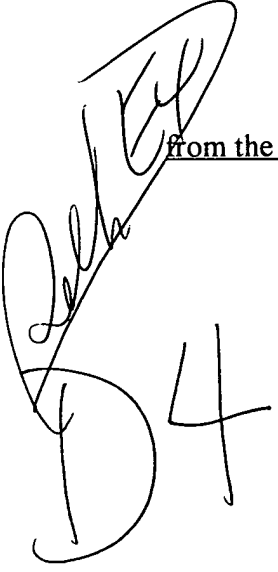
151. A method according to claim 150 wherein said viral vector is administered by means of infection or liposome mediated transfection.

152. A method according to claim 144 wherein said DNA vector is a plasmid.

153. A method according to claim 152 wherein said plasmid is administered by means of liposome mediated transfection or as naked DNA.

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154. A method of expressing an OB polypeptide in a mammal comprising

administering to said mammal a mammalian cell comprising an expression vector which vector comprises DNA encoding an OB polypeptide capable of modulating body weight operatively associated with an expression control sequence, under conditions that provide for expression of the OB polypeptide by the mammal.

 155. A method according to claim 154 wherein said OB polypeptide is selected from the group consisting of:

- a) the amino acid sequence set out in SEQ ID NO: 2;
- b) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 2;
- c) the amino acid sequence set out in SEQ ID NO: 4;
- d) the amino acid sequence set out in amino acids 22-167 of SEQ. ID. NO: 4;  
and
- e) variants, including allelic variants, muteins, analogs and fragments of any of subparts (a) through (d), capable of modulating body weight.

156. A method according to claim 155 wherein said OB polypeptide variant is selected from the group consisting of the amino acid sequence set forth in:

- a) SEQ ID NO: 5;
- b) amino acids 22-166 of SEQ ID NO: 5;
- c) SEQ ID NO: 6; and
- d) amino acids 22-166 of SEQ ID NO: 6.

157. A method according to claim 154 wherein said OB polypeptide has 83 percent or greater amino acid sequence homology to the OB polypeptide amino acid sequence set out in SEQ ID NOS: 2, 4 / 5 or 6.

158. A method according to claim 155 wherein said OB polypeptide has one or more amino acids selected from the group consisting of amino acids 53, 56, 71, 85, 89, 92, 95, 98, 110, 118, 121, 122, 126, 127, 128, 129, 132, 139, 157, 159, 163 and 166, according to the

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numbering of SEQ ID NO: 4, substituted with another amino acid.

159. A method according to claim 156 wherein said OB polypeptide has one or more of amino acids selected from the group consisting of amino acids 52, 55, 70, 84, 88, 91, 94, 97, 109, 117, 120, 121, 125, 126, 127, 128, 131, 138, 156, 158, 162 and 165, according to the numbering of SEQ ID NO: 6, substituted with another amino acid.

160. A method according to claims 144 or 154 wherein said expression control sequence is selected from the group consisting of the early or late promoters of SV40, CMV, vaccinia, polyoma and adenovirus and the promoter for 3-phosphoglycerate kinase and other glycolytic enzymes.

*D4*  
161. A method of activating the expression of endogenous nucleic acid encoding an OB polypeptide by means of a homologous recombinational event consisting of inserting an expression regulatory sequence in functional proximity to the OB polypeptide encoding sequence.

162. A method for modifying the body weight of a mammal comprising administering to said mammal a mammalian cell comprising an OB polypeptide encoding DNA sequence and modified *in vitro* to permit higher expression of OB polypeptide by means of a homologous recombinational event consisting of inserting an expression regulatory sequence in functional proximity to the OB polypeptide encoding sequence.

#### REMARKS

The foregoing amendments and the following remarks are submitted in response to the Office action mailed September 24, 1997.

The Examiner has objected to the specification at page 155, line 16 as lacking the specific